510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
DEVICE ONLY TEMPLATE

A. 510(k) Number:
k033415

B. Analyte:
Methicillin Resistant Staphylococcus aureus (MRSA) detection

C. Type of Test:
Nucleic Acid Amplification Test, DNA, Methicillin Resistant Staphylococcus aureus (MRSA), qualitative

D. Applicant:
Infectio Diagnostic (I.D.I.) Inc.

E. Proprietary and Established Names:
IDI-MRSA™ Assay

F. Regulatory Information:

1. Regulation section:
   866.1640
2. Classification:
   II
3. Product Code:
   NQX
4. Panel:
   83

G. Intended Use:

1. Intended use(s):
   IDI-MRSA™ is a qualitative *in vitro* diagnostic test for the direct detection of nasal colonization by methicillin-resistant *Staphylococcus aureus* (MRSA) to aid in the prevention and control of MRSA infections in healthcare settings. The test performed on the Smart Cycler® instrument with a nasal swab specimen from patients at risk for colonization, utilizes polymerase chain reaction (PCR) for the amplification of MRSA DNA and fluorogenic target-specific hybridization probes for the detection of the amplified DNA.

   IDI-MRSA™ is not intended to diagnose MRSA infections nor to guide or monitor treatment for MRSA infections. Concomitant cultures are necessary only to recover organisms for epidemiological typing or for further susceptibility testing.

2. Indication(s) for use:
   IDI-MRSA™ can be used to establish MRSA colonization.
3. Special condition for use statement(s):
   Prescription use only.
4. Special instrument Requirements:

H. Device Description:

IDI-MRSA™ is a qualitative *in vitro* diagnostic test for the direct detection of nasal colonization by methicillin-resistant *Staphylococcus aureus* (MRSA). A nasal specimen is collected and transported to the laboratory using the Copan Venturi Transystem®. The test is assayed directly from the clinical specimen, in this case a nasal swab. It is performed on the Smart Cycler®, a random-access analyzer that automates in a closed-tube assay, the denaturation, hybridization, and amplification of DNA. The decision algorithm for interpretation of IDI-MRSA™ assay is automated using diagnostic software on the Smart Cycler® instrument. The assay includes:

- Internal Control- a DNA sequence (not found in MRSA) that is co-amplified with the specimen and is intended to monitor for specimen inhibition and the integrity of assay reagents.
- Positive Control – an external control that is intended to monitor for reagent failure
- Negative Control – an external control that is intended to monitor for reagent or environmental contamination.

I. Substantial Equivalence Information:

1. Predicate device name(s):
   PBP2' Latex Agglutination Test (Oxoid)
2. Predicate K number(s):
   K011710
3. Comparison with predicate:

Similarities		
Item	**Device**	**Predicate**
Intended use	Qualitative test for detecting MRSA	Qualitative test for detecting MRSA
Differences		
Item	**Device**	**Predicate**
Mode of detection	Presence of SCC*mec* cassette (genetic element that carries the *mecA* gene) at orflX junction (specific to *S. aureus*).	Detection of the penicillin-binding protein PBP2', a protein expressed by the *mecA* gene.
Specimen type	Nasal swab	Isolated colonies of *S. aureus*
Assay format	Amplification: PCR Detection: Fluorogenic target-specific hybridization	Agglutination with latex particles sensitized with monoclonal antibody against PBP2'

Reading of results	Automated using diagnostic software on the Smart Cycler®	Visual readings
Time from specimen collection to available result	Within 1 hour	Between 16 hour and 48 hour.

J. Standard/Guidance Document Referenced (if applicable):
Not Applicable

K. Test Principle:
IDI-MRSA™ is a qualitative in vitro diagnostic test using polymerase chain reaction (PCR) technology for the detection of DNA sequencing that is associated with methicillin resistant Staphylococcus aureus (MRSA). The IDI-MRSA™ does not detect *mecA* or it's by product PBP2'directly. The IDI-MRSA™ targets the *Staphylococcus aureus* species specific orfX sequence and a sequence of SCCmec near the integration site and not a *mecA* sequence specifically. The test is done directly from the clinical specimen, in this case a nasal swab. It is performed on the Smart Cycler®, a random-access analyzer that automates in a closed-tube assay (tube does not need to be opened following amplification in order to do the detection of amplicons) the denaturation, hybridization and elongation of the PCR reaction as well as the fluorometric detection of the amplified DNA. The Smart Cycler® instrument monitors simultaneously the fluorescence emitted by the reaction.

L. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. Precision/Reproducibility:

A panel of 10 simulated specimens with varying concentrations of MRSA and the two controls (positive and negative) of the IDI-MRSA™ assay were tested in triplicate on three different days at each site (10 specimens plus two controls tested in triplicate on 3 days at 3 sites). This was repeated with three lots of reagents.

Specimen ID	Lot 1	Lot 2	Lot 3	Total agreement (%)
negative	27/27	27/27	27/27	81/81 (100%)
negative	27/27	27/27	27/27	81/81 (100%)
Weak pos.[A]	19/27	18/27	16/27	53/81 (65%)
Strong pos.	27/27	27/27	27/27	81/81 (100%)
Strong pos.	27/27	27/27	27/27	81/81 (100%)
Weak pos.[A]	14/27	13/27	18/27	45/81 (56%)
Positive	27/27	27/27	27/27	81/81 (100%)
Positive	27/27	27/27	27/27	81/81 (100%)
Weak pos.	27/27	27/27	27/27	81/81 (100%)
Positive	27/27	27/27	27/27	81/81 (100%)
Pos. control	26/27	27/27	27/27	80/81 (99%)
Neg. control	26/27	27/27	27/27	80/81 (99%)
Total agreement (%)	301/324 (93%)	301/324 (93%)	304/324 (94%)	906/972 (93%)

[A] Specimens with CFUs below the limit of detection of the assay.

b. Linearity/assay reportable range:
Not applicable.

c. Traceability (controls, calibrators, or method):
Controls: The following three controls monitor either directly or indirectly all aspects of the test except for the cell lysis and DNA extraction.

- Internal Control (IC) monitors for the presence of inhibitory substances in the assay tube, indicated by a failed internal control. It also ensures that reaction conditions (temperature, time) of each step of the PCR in that tube are acceptable for the amplification reaction and that the reagents are functional. Not all primers and probes are controlled by the IC but it can be a general control. If IC fails the report will say "unresolved"
- Positive control is an assay run control. In conjunction with the IC it is used to verify reagent and system functionality.
- Negative control is an assay run control also. It detects reagent or environmental contamination by either MRSA or MRSA amplicons.

To monitor cell lysis and DNA extraction, a recommendation is placed in the Package Insert to test external controls.

d. Detection limit:
The analytical sensitivity (limit of detection or LOD) of IDI-MRSA™ assay was determined with 7 strains of MRSA. Quantitated culture and purified genomic DNA diluted in the sample preparation buffer of IDI-MRSA™ assay were tested in 5 replicates. The LOD is defined as the smallest concentration at which at least 92.5% of all replicates test positive. The LOD of IDI-MRSA™ assay is 15 genome copies per reaction. The LOD in CFU is 5 CFU/reaction. Taking into account the dilution factor due to specimen processing, this translates into approximately 325 CFU/swab.

e. Analytical specificity:
Genomic DNA from 37 ATCC strains representing species phylogenetically related to *S. aureus* and members of the nasal commensal flora, 27 strains (15 reference strains and 12 clinical isolates) of methicillin-sensitive coagulase negative staphylococci and 44 strains (two reference strains and 42 clinical isolates) of methicillin-resistant coagulase negative staphylococci were tested. The specificity was 100%.

f. Assay cut-off:
In order to reach the highest sensitivity for IDI-MRSA™, the cut-off values were set at their lowest possible value, that is, the endpoint threshold at a value of 15 and the 2nd derivative peak threshold at a value of 20.

2. Comparison studies:

a. Method comparison with predicate device:

Performance characteristics of IDI-MRSA™ assay were determined in a multi-site (4 medical centers) prospective investigational study. Patients enrolled in the study included but were not necessarily limited to: systematic screening of all patients at admission, prior MRSA infection or carriage, transfer from another institution, prolonged hospital stay or history of prolonged hospitalization and contact with an MRSA carrier but had not received antibiotic therapy for MRSA. In total, 786 nasal specimens collected with the Copan Venturi Transystem® (Copan Diagnostics Inc, Corona, CA) were screened for MRSA with the culture method of reference and with IDI-MRSA™ assay.

The reference method consisted of an initial analysis with the oxacillin screen agar test after selective growth on mannitol salt agar. Specimens negative for MRSA were subjected to an additional analysis consisting of an enrichment step in trypticase soy broth (TSB) containing 6.5% NaCl followed by the oxacillin screen agar test. An MRSA culture-positive specimen was defined as a specimen positive for MRSA by either culture technique. An MRSA culture-negative specimen was defined as a specimen negative for MRSA by both culture techniques.

For the screening method with selective growth on mannitol salt agar (MSA), plates were directly inoculated with nasal swab specimens followed by incubation at 35°C for 24 to 48 hours. When necessary, presumptive colonies of *S. aureus* were subcultured to 5% sheep blood agar plates and incubated for 24-48 hours at 35°C. Otherwise isolated colonies were tested directly from MSA plates. Presumptive staphylococcal colonies were confirmed with a latex agglutination assay or by a tube coagulase test. Confirmed *S. aureus* colonies were tested on Mueller-Hinton agar plate supplemented with oxacillin (6 μg/mL) and NaCl (4% w/v) incubated at 33 to 35°C (not exceeding 35°C) for a full 24 hours. MRSA screening with an enrichment step in tryptic soy broth (TSB) containing 6.5% NaCl was also performed in cases where a negative result for MRSA was obtained with the MSA screening method. Confirmation of presumptive colonies and determination of methicillin resistance were done as described above.

Compared to the culture reference methods described above, the IDI-MRSA™ identified 92.5% of the specimens positive for MRSA by either culture method and 96.4% of the specimens negative by both culture methods. For the population tested, this results in a negative predictive value of 98.2% and a positive predictive value of 85.4%.

Table 1. Results obtained with IDI-MRSA™ assay in comparison to the reference method[1].

		IDI-MRSA™		
		Positive	Negative	Total
Culture techniques	Positive	135	11	146
	Negative	23	609	632
	Total	158	620	778

Eight (8) specimens that gave initially unresolved results remained unresolved upon retesting with IDI-MRSA™ assay and are not included in the table. All 8 were culture negative.

Fourteen of the 23 IDI-MRSA™ positive results that were reference culture negative were further evaluated and determined to be culture positive by additional testing.

b. Matrix comparison:
Not applicable

3. Clinical studies:
   a. Clinical sensitivity:
   Not applicable
   b. Clinical specificity:
   Not applicable
   c. Other clinical supportive data (when a and b are not applicable):
   Not applicable
4. Clinical cut-off:
   Not applicable
5. Expected values/Reference range:
   In the investigational study for IDI-MRSA™ assay, the overall *S. aureus* nasal carriage rate determined by culture (*S. aureus* isolated in specimens by either culture technique) was 36.1% with a range of 33-40%. Fifty one percent (51%) of *S. aureus* isolates were methicillin resistant by the oxacillin screen agar method [Mueller-Hinton agar plate supplemented with oxacillin (6 μg/mL) and NaCl (4% w/v)] for an overall MRSA nasal carriage rate of 18.6%. With IDI-MRSA™ assay, the overall MRSA nasal carriage rate was 20.3%.

M. Conclusion:

The IDI-MRSA™ assay for Methicillin Resistant Staphylococcus aureus (MRSA) detection is substantially equivalent to the predicate PBP2' Latex Agglutination Test (Oxoid) for the detection of MRSA.